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EXAMINER

CHONG, KIMBERLY

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 09/847,601	Applicant(s) LEWIN ET AL.	
	Examiner Kimberly Chong	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 27 March 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-59 is/are pending in the application.
- 4a) Of the above claim(s) 2,3,5-7,9-13 and 43-47 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4,8,14-42 and 59 is/are rejected.
- 7) ☒ Claim(s) 1,4 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 03/27/2007 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 09/27/2006 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed on 03/27/2007, claims 1-59 are pending in the application. Claims 1, 4, 8, 14-42 and 58-59 are currently under examination and claims 2-3, 5-7, 9-13 and 43-57 are withdrawn as being drawn to a non-elected invention.

Applicants note that no rejections were raised against claims 58 and 59 in the Office action filed 09/27/2006 and therefore these claims should now be considered allowable. While it is true that claim 59 was inadvertently left out of the recitation of rejected claims on page 14, the subject matter of claim 59 was clearly rejected i.e. a ribozyme that specifically cleaves an mRNA comprising the sequence of SEQ ID No. 58 and claim 58 was recited as rejected on PTO Form 326. Thus, the claim 59 was in fact rejected in the last Office action mailed 09/27/2006. Claim 58 is free of the prior art searched and of record.

Claim Objections

Claims 1 and 4 are objected to as reciting non-elected subject matter. Claims 1 and 4 should be rewritten deleting any non-elected subject matter.

Claim 4 is objected to as being dependent upon a withdrawn base claim and reciting non-elected subject matter, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims and deleting non-elected subject matter. Claim 4 still contains non-elected subject matter i.e SEQ ID No. 101.

New Claim Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 8, 14-42 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wright et al. (of record), Thompson et al. (of record), Pavco et al. (of record) and Kido et al. (of record).

The instant claims are drawn to a ribozyme that specifically cleaves an mRNA encoding an IGF-1 receptor polypeptide that causes or contributes to the disease, disorder, or dysfunction of a cell or a tissue of a mammalian eye (claim 1), wherein the

ribozyme specifically cleaves an mRNA that comprises a nucleotide sequence having SEQ ID No. 88, (claim 1 and 59), wherein the ribozyme is a hammerhead or hairpin ribozyme (claims 14-15) and further drawn to a vector comprising a polynucleotide encoding said ribozyme and a promoter (claim 16). The instant claims are further drawn to a host cell, wherein said host cell is mammalian or a human cell (claims 30-32) and drawn to a composition, wherein said composition further comprises a pharmaceutical excipient (claims 36-37 and 39) and drawn to a kit wherein said kit comprises a composition (claims 40-41).

Wright et al. teach an antisense oligonucleotide that binds to and inhibits expression of a sequence comprising SEQ ID NO. 88 (see sequence alignment, IGF-I oligonucleotide #2501, of record 09/27/2006) and teach IGF-1, also known as Type 1 or IGF-1 receptor, is involved in neovascularization of the retina (see page 21, lines 6-15). Wright et al. does not teach the oligonucleotide is a ribozyme and further does not teach a vector comprising a promoter and a ribozyme, a host cell comprising a ribozyme, a composition or a kit comprising a ribozyme and further do not teach a delivery device, such as filter disks surgically implanted into a mammalian eye for delivery of said ribozyme composition nor teach a vector wherein said promoter element directs expression of said polynucleotide in a retinal cell, a photoreceptor cell, a rod or cone cell, a Mueller cell or wherein said promoter comprises a mammalian rod opsin promoter element.

Thompson et al. teach ribozyme molecules and teach the enzymatic nature of ribozymes is advantageous over technologies such as antisense technologies (see col.

2). Thompson et al. further teach ribozymes can be hammerheads or hairpins (see col. 13), teach expression vectors comprising promoters and ribozymes (see col. 8), and teach pharmaceutical compositions comprising liposomes and ribozymes (see col. 10).

Pavco et al. teach a viral vector, specifically an adeno-viral vector, comprising a ribozyme (see col. 6 and 13, lines 33-52 and 36-60, respectively) and teach the use of viral particles comprising said ribozyme to deliver said ribozyme to target cells (see col. 14, lines 1-15). Pavco et al. additionally teach human host cells comprising said ribozymes and teach compositions comprising lipofectamine and said ribozymes (see Example 2). Further, Pavco et al. teach use of ribozyme as diagnostic reagents and further teach a delivery device, such as filter disks surgically implanted into a mammalian eye for delivery of said ribozyme composition (see col. 21 and Example 11).

Kido et al. teach use of a viral vector comprising a mouse opsin promoter (see Figure 1). Kido et al. teach said opsin promoter directs expression in photoreceptor cells, which comprise rod and cone cells, and directs expression in Mueller cells (see page 838 second column and Figure 8C).

It would have been obvious to one of skill in the art to substitute a ribozyme for an antisense molecule, as taught by Thompson et al., to inhibit expression of a gene encoding IGF-I receptor, a polypeptide involved in neovascularization of the retina, as taught by Wraight et al. It would have been further obvious to one of ordinary skill in the art to incorporate the mammalian opsin promoter, as taught by Kido et al. into a viral vector expressing a ribozyme targeted to cells of a mammalian eye, as taught by Pavco et al. and Thompson et al.

One of skill in the art would have been motivated to use a ribozyme molecule to target IGF-I instead of an antisense, because Thompson et al. and Pavco et al. both teach ribozymes are advantageous over antisense oligonucleotides since the effective concentration of ribozymes necessary to effect therapeutic treatment is lower than that of antisense oligonucleotides (see col. 2). Further, one of skill in the art would have been motivated to use a ribozyme because the ribozyme is a highly specific inhibitor and has the ability to act enzymatically: a single ribozyme molecule is able to cleave many molecules of a target RNA. One of skill in the art would have clearly been motivated to incorporate a mammalian opsin promoter because Kido et al. teach a viral vector comprising an opsin promoter is capable of selectively directing expression of therapeutic genes to photoreceptor cells (see page 841, last paragraph). One of skill in the art would want to make a vector comprising an opsin promoter to specifically express ribozymes targeted to VEGF in retinal cells for the purpose of decreasing expression of VEGF, which contributes to disease of the eye, such as retinopathy. Additionally, it would have been obvious to one of skill in the art and one would have been motivated to package the ribozyme in a kit because Pavco et al. specifically teach ribozymes targeted eye diseases would be useful as a diagnostic reagent and teach specific embodiments of treatment with a ribozyme delivered on a filtered disk to the cornea of a rat and therefore would have had a reasonable expectation of success.

Finally, one would have had a reasonable expectation of success at making a ribozyme targeted to IGF-I given that the IGF-I sequence was known, as evidenced by Wraight et al. making specific inhibitory sequences targeted to IGF-I, and further given

that Thompson et al. provides a detailed disclosure of how to make any ribozyme targeted to any sequence. One would have also had a reasonable expectation of success given that Kido et al. teach an opsin promoter incorporated into a vector directs expression of a gene in retinal cells, specifically photoreceptors and Mueller cells.

Thus, in absence of evidence to the contrary, the invention would have been *prima facie* evident to one of ordinary skill in the art.

The foregoing represents a new rejection necessitated by claim amendments filed 03/27/2007 however, response to applicant's arguments will be addressed since they would apply to the new grounds of rejection above.

Applicant's argue in the remarks filed 03/27/2007 that none of the references provide any guidance about selecting particular sequences from within an mRNA encoding an IGF-1 receptor polypeptide, none of the references teach or suggest actual target sequences within the IGF-1 receptor encoding RNA, none of the references teach or suggest the use of target sequences within the mRNA to create particular ribozyme sequences that would cleave any such mRNAs and none of the references teach or suggest particular ribozyme sequences that would cleave any such mRNAs. Therefore, the references cannot render the claimed invention obvious and there is not teaching, suggestion or motivation in identifying specific nucleotide sequences of an IGF-1 receptor to target.

In response to the references not providing any guidance about selecting particular sequences from with an IGF-1 mRNA receptor polypeptide or the use of the

target sequence to create particular ribozymes, the claims are not drawn to providing any guidance about selecting an appropriate sequence within an IGF-1 mRNA polypeptide nor are the claims drawn to the use of the target sequence to make particular ribozyme sequences. The instant claims are drawn to a ribozyme that cleaves an mRNA encoding an IGF-1 receptor polypeptide wherein the target comprises SEQ ID No. 88. Wraight et al. teach an antisense sequence targeted to a gene encoding SEQ ID No. 88 and both Thompson et al. and Pavco et al. teach how to make and use any ribozyme to any target sequence and teach the advantages of using ribozymes for cleaving target mRNA. Therefore, absent evidence to the contrary, it would have been obvious to make a ribozyme capable of targeting and cleaving a mRNA encoded by a gene comprising SEQ ID NO. 88, as taught by Wraight et al. Applicants argument that none of the references teach the claimed target sequence; applicant is directed to the sequence alignment provided in the Office action mailed 09/27/2006 wherein Wraight et al. teach a target sequence comprising SEQ ID No. 88 and teach an antisense compound complementary to said target sequence. In response to applicant's argument that none of the references teach or suggest the claimed ribozyme sequences, the instantly rejected claims are not drawn to a particular ribozyme sequence that targets a gene encoding IGF-1 receptor and therefore it was not necessary to reject such sequences.

Therefore, the instant invention was obvious to one of skill in the art.

Response to Applicant's Arguments

Re; Double Patenting

The terminal disclaimer filed on 03/27/2007 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent No. 6,225,291 has been reviewed and is accepted. The terminal disclaimer has been recorded. As such, the rejection under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1-3, 9-15, 17-20 and 22-38 of U.S. Patent No. 6,225,291 is moot.

Re: Claim Rejections - 35 USC § 112

The rejection of record mailed 09/27/2006 of claims 1 and 14-42 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is obviated in response to claim amendments filed 03/27/2007.

Re: Claim Rejections - 35 USC § 102

The rejection of record mailed 09/27/2006 of claims 1, 14, 30-34 and 36-39 are rejected under 35 U.S.C. 102(a) as being anticipated by Caballero et al. (Investigative Ophthalmology and Visual Science 1991) is obviated in response to claim amendments filed 03/27/2007.

The rejection of record mailed 09/27/2006 of claims 1, 14-18, 24-33 and 36-39 rejected under 35 U.S.C. 102(e) as being anticipated by Pavco et al. (U.S. Patent No. 6,346,398) is obviated in response to claim amendments filed 03/27/2007.

Claim Rejections - 35 USC § 103

The rejection of record of claims 1, 8, 14-16, 30-32, 36-37 and 39-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wraight et al. (WO 00/78341) and Thompson et al. (U.S. Patent No. 5,750,390) is maintained for the reasons of record mailed in the Office action 09/27/2006. Response to applicant's arguments is above in the new grounds of rejection.

The rejection of record mailed 09/27/2006 of claims 1 and 14-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pavco et al. (U.S. Patent No. 6,346,398) and Kido et al. (Current Eye Research 1996) is obviated in response to claim amendments filed 03/27/2007.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

Art Unit: 1635

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

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Kimberly Chong
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